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Dear Pap:

I am sorry to have been so slow in answering your letter and reading the accompanying papers, but I have been held up both by proof and by urgent reading for one or two colleagues here.

The antitoxin work is extremely interesting, and certainly supports your contention of a partial splitting of the molecule. But can the dissymetry figures be taken so literally that one can be sure which way the molecule is split? Couldn't a bite be taken out like  , followed by a more symmetrical redistribution? It is interesting, too, that the inactive protein in the fraction should behave similarly on digestion.

Your preliminary experiments on the Pn antibody digestion show that that could be profitably followed up, too. We have made a run on the Albany serum, too, and find at least 3 heavy components. I suppose no two horses behave alike toward Pn. What is more, the antibody is in the $\gamma$-fraction of this serum, so that we now have heavy and light horse antibodies in either a separate component, or moving with the $\gamma$-fraction. It's all very complicated, and as you say, the Fell et al paper contributes nothing but confusion. Your suggestion about the activity of enzymes in the clot is a possible lead out of the maze. I wish you could go ahead on it, also on making the horse antibodies fit for democracy.

As for Pauling's theory, as he has expressed it, the active groups are on the ends of the molecule but I do not see why they should have to be. His theory will need to be and can easily be modified in a number of respects. I wrote him your work had a bearing on his theory and that I was encouraging you to write him, which I now do. I think he'll take it in good part. I disagree with many points that he stresses, such as limiting the

"valence" of antibodies to two, and also to the one about strong groups. Our phosphorylated proteins are not worse antigens than the P-free analogs.

Sincerely,

MH/m

Michael Heidelberger.